S/N Unknown PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Clague P. Hodgson	Examiner: Unknown
Serial No.:	Unknown	Group Art Unit: Unknown
Filed:	Herewith	Docket: 518.001US2
Title:	VECTORS FOR GENE TRANSFER	
	(Continuation Under 1.53(b) of Serial No. 08/522,336, filed November 9, 1995)	

PRELIMINARY AMENDMENT

Commissioner for Patents
Washington, D.C. 20231

Prior to examination, please amend the above-identified continuation application as follows.

In the Title

Please change the title to read: --VECTORS FOR GENE TRANSFER--.

In the Specification

On page 1, after the title, please add the following section:

--RELATED APPLICATIONS

This is a Continuation Under 1.53(b) of U.S. Application Serial No. 08/522,336, filed November 9, 1995, which is U.S. National Stage filing under 35 U.S.C. 371 of PCT/US94/02752, filed March 14, 1994 (published as WO 94/20608 on September 15, 1994), which applications are incorporated herein by reference.--

In the Abstract

Please insert the Abstract attached hereto on a separate sheet.

In the Claims

Please cancel claims 1-76.

Please add the following new claims 77-87:

77. A method of expressing a DNA sequence into an animal comprising:

(a) introducing a DNA transfer vector into a donor cell to yield a transformed

donor cell, wherein the DNA transfer vector comprises linked:

(i) a 5′ long terminal repeat (LTR) sequence derived from a retrotransposon comprising a transcription initiation site for RNA;

(ii) an encapsidation sequence positioned 3′ of the 5′ LTR;

(iii) a primer binding site sequence positioned 3′ of the 5′ LTR;

(iv) a 3′ LTR sequence derived from a retrotransposon positioned 3′ of the primer binding site which includes:

(1) sequences necessary for polyadenylation of a RNA transcript initiated in the 5′ LTR;

(2) sequences necessary for reverse transcription of the RNA transcript from step (d)(1) into a double stranded cDNA;

(v) a polypurine tract sequence located 5′ to the 3′ LTR;

(vi) a DNA sequence comprising at least one open reading frame inserted into the vector 3′ of the transcription initiation site in the 5′ LTR of the vector; and

(vii) sequences within each LTR which are necessary for integration of the vector into the genome of a cell, wherein the vector sequences of i), ii), iii), iv) and v) comprise no more than 2 kbp;

(b) introducing the transformed donor cell to an organ of an animal, tissue of an animal, an embryo of an animal or an animal; and

(c) identifying a cell in the organ, tissue, embryo or animal which expresses the DNA sequence of (a)(vi).

78. The method of claim 77 wherein the donor cell is an embryonic stem cell, a pluripotent stem cell, or an embryo.

79. The method of claim 77 wherein the donor cell is a bone marrow cell which is first treated with mycophenolic acid to render it quiescent, and then treated with a cytokine to induce proliferation.

80. A method of expressing a DNA sequence into an animal comprising:

(a) introducing a DNA transfer vector into a donor cell capable of packaging nucleic acid molecules into a virion to yield a transformed donor cell, wherein the DNA transfer vector comprises linked:

(i) a 5′ long terminal repeat (LTR) sequence derived from a retrotransposon comprising a transcription initiation site for RNA;

(ii) an encapsidation sequence positioned 3′ of the 5′ LTR;

(iii) a primer binding site sequence positioned 3′ of the 5′ LTR;

(iv) a 3′ LTR sequence derived from a retrotransposon positioned 3′ of the primer binding site which includes:

(1) sequences necessary for polyadenylation of a RNA transcript initiated in the 5′ LTR;

(2) sequences necessary for reverse transcription of the RNA transcript from step (d)(1) into a double stranded cDNA;

(v) a polypurine tract sequence located 5′ to the 3′ LTR;

(vi) a DNA sequence comprising at least one open reading frame inserted into the vector 3′ of the transcription initiation site in the 5′ LTR of the vector; and

(vii) sequences within each LTR which are necessary for integration of the vector into the genome of a cell, wherein the vector sequences i), ii), iii), iv) and v) comprise no more than 2 kbp;

(b) introducing the transformed donor cell to an organ of an animal, tissue of an animal, an embryo of an animal or an animal; and

(c) identifying a cell in the organ, tissue, embryo or animal which expresses the DNA sequence of (a)(vi).

81. A method of producing a double-stranded cDNA containing a gene which is capable of homologous recombination with the genome of a cell, comprising:

(a) introducing a DNA transfer vector into a donor cell to yield a transformed donor cell, wherein the DNA transfer vector comprises linked:

(i) a 5′ long terminal repeat (LTR) sequence derived from a retrotransposon comprising a transcription initiation site for RNA;

(ii) an encapsidation sequence positioned 3′ of the 5′ LTR;

(iii) a primer binding site sequence positioned 3′ of the 5′ LTR;

(iv) a 3′ LTR sequence derived from a retrotransposon positioned 3′ of the primer binding site which includes:

(1) sequences necessary for polyadenylation of a RNA transcript initiated in the 5′ LTR;

(2) sequences necessary for reverse transcription of the RNA transcript from step (d)(1) into a double stranded cDNA;

(v) a polypurine tract sequence located 5′ to the 3′ LTR;

(vi)a DNA sequence inserted into the vector 3′ of the transcription initiation site in the 5′ LTR of the vector which DNA sequence comprises a polyd(T) tract 3' to an open reading frame which is capable of homologous recombination with the genome of the cell; and

(vii) sequences within each LTR which are necessary for integration of the vector into the genome of a cell, wherein the vector sequences of i), ii), iii), iv) and v) comprise no more than 2 kbp; and

(b) identifying a cell which contains an integrated form of the vector comprising the DNA sequence which is capable of homologous recombination with the genome of the cell.

82. A method of reconstituting tissues with genetically modified embryonic stem cells comprising:

(a) introducing a DNA transfer vector into an embryonic stem cell to yield a transformed embryonic stem cell, wherein the DNA transfer vector comprises linked:

(i) a 5′ long terminal repeat (LTR) sequence derived from a retrotransposon comprising a transcription initiation site for RNA;

(ii) an encapsidation sequence positioned 3′ of the 5′ LTR;

(iii) a primer binding site sequence positioned 3′ of the 5′ LTR;

(iv) a 3′ LTR sequence derived from a retrotransposon positioned 3′ of the primer binding site which includes:

(1) sequences necessary for polyadenylation of a RNA transcript initiated in the 5′ LTR;

(2) sequences necessary for reverse transcription of the RNA transcript from step (d)(1) into a double stranded cDNA;

(v) a polypurine tract sequence located 5′ to the 3′ LTR;

(vi) a DNA sequence comprising an open reading frame inserted into the vector 3′ of the transcription initiation site in the 5′ LTR of the vector; and

(vii)sequences within each LTR which are necessary for integration of the vector into the genome of a cell, wherein the vector sequences of i), ii), iii), iv) and v) comprise no more than 2 kbp;

(b) introducing the transformed donor cell to an organ of an animal, tissue of an animal, an embryo of an animal or an animal; and

(c) identifying a cell in the organ, tissue, embryo or animal which comprises the DNA sequence of (a)(vi).

83. The method of claim 82 wherein the embryonic stem cell has been modified with respect to the histocompatibility antigens present on the stem cell surface.

84. A method of preparing genetically modified embryonic stem cells comprising:

(a) introducing a DNA transfer vector into an embryonic stem cell to yield a transformed embryonic cell, wherein the DNA transfer vector comprises linked:

(i) a 5′ long terminal repeat (LTR) sequence derived from a retrotransposon comprising a transcription initiation site for RNA;

(ii) an encapsidation sequence positioned 3′ of the 5′ LTR;

(iii) a primer binding site sequence positioned 3′ of the 5′ LTR;

(iv) a 3′ LTR sequence derived from a retrotransposon positioned 3′ of

the primer binding site which includes:

(1) sequences necessary for polyadenylation of a RNA transcript initiated in the 5′ LTR;

(2) sequences necessary for reverse transcription of the RNA transcript from step (d)(1) into a double stranded cDNA;

(v) a polypurine tract sequence located 5′ to the 3′ LTR;

(vi) a DNA sequence comprising an open reading frame inserted into the vector 3′ of the transcription initiation site in the 5′ LTR of the vector; and

(vii) sequences within each LTR which are necessary for integration of the vector into the genome of a cell, wherein the vector sequences of i), ii), iii), iv) and v) comprise no more than 2 kbp; and

(b) identifying a transformed embryonic stem cell which comprises the DNA sequence.

85. A method of delivering an autonomously replicating DNA sequence to the genome of a recipient cell comprising:

(a) introducing a DNA transfer vector into a donor cell to yield a transformed donor cell, wherein the DNA transfer vector comprises linked:

(i) a 5′ long terminal repeat (LTR) sequence derived from a retrotransposon comprising a transcription initiation site for RNA;

(ii) an encapsidation sequence positioned 3′ of the 5′ LTR;

(iii) a primer binding site sequence positioned 3′ of the 5′ LTR;

(iv) a 3′ LTR sequence derived from a retrotransposon positioned 3′ of the primer binding site which includes:

(1) sequences necessary for polyadenylation of a RNA transcript initiated in the 5′ LTR;

(2) sequences necessary for reverse transcription of the RNA transcript from step (d)(1) into a double stranded cDNA;

(v) a polypurine tract sequence located 5′ to the 3′ LTR;

(vi) a DNA sequence comprising an autonomously replicating DNA sequence inserted into the vector 3′ of the transcription initiation site in the 5′ LTR of the vector; and

(vii) sequences within each LTR which are necessary for integration of the vector into the genome of a cell, wherein the vector sequences of i), ii), iii), iv) and v) comprise no more than 2 kbp; and

(B) identifying a transformed cell which contains the DNA sequence of (a)(vi).

86. A method of increasing the resistance of a cell to infection by a retrovirus comprising introducing at least one retrotransposon-derived vector that is transcribed at a high efficiency into the cell so that following infection by the retrovirus, RNA transcribed in the cell from the retrotransposon vector outcompetes RNA derived from the retrovirus for packaging proteins or cellular translational machinery.

87. The method of claim 86 wherein the vector comprises linked:

(i) a 5′ long terminal repeat (LTR) sequence derived from a retrotransposon comprising a transcription initiation site for RNA;

(ii) an encapsidation sequence positioned 3′ of the 5′ LTR;

(iii) a primer binding site sequence positioned 3′ of the 5′ LTR;

(iv) a 3′ LTR sequence derived from a retrotransposon positioned 3′ of the primer binding site which includes:

(1) sequences necessary for polyadenylation of a RNA transcript initiated in the 5′ LTR;

(2) sequences necessary for reverse transcription of the RNA transcript from step (d)(1) into a double stranded cDNA;

(v) a polypurine tract sequence located 5′ to the 3′ LTR; and

(vi) sequences within each LTR which are necessary for integration of the vector into the genome of a cell, wherein the vector sequences of i), ii), iii), vi) and v) comprise no more than 2 kbp.

Remarks

Original claims 1-76 have been cancelled, and new claims 77-87 added.

The Examiner is invited to telephone Applicant's attorney (612-373-6959) to facilitate prosecution of this application.

If necessary please charge any additional fees or credit overpayment to Deposit Account No. 19-0743.

Respectfully submitted,

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